

second law of heat to protein systems has, in some quarters,* been questioned. In considering the *electrochemical* behavior of the proteins I have assumed the applicability of Arrhenius' hypothesis of electrolytic dissociation, of Kolrausch's law of the independent motion of ions, of the Nernst theory of concentration-cells, and further, although this has of recent years been very strongly questioned,† the applicability of the Guldberg and Waage mass-law to reactions between ions. I believe that the utility of these hypotheses justifies us in applying them until still more useful hypotheses shall have been elaborated to amplify or replace them.

A previous edition of this work appeared, in German, six years ago.‡ Since that time our knowledge of the physico-chemical behavior of the proteins has very considerably expanded and increased in exactitude. Among the particularly important investigations which have appeared during this period may be mentioned the invention by Van Slyke of an accurate and simple method of determining free amino-groups (Cf. Chapter I), the work of Pauli upon the combining-capacity of deaminized proteins (Cf. Chapters I, VIII and IX), the work of Schmidt and of af Ugglas upon compound proteins (Cf. Chapter VII), the work of Procter upon the swelling of protein jellies (Cf. Chapter XII), the work of Reichert and Brown upon the crystallography of hæmoglobin (Cf. Chapter XII) and that of Dabrowsky upon the molecular volumes of proteins dissolved in water and in solutions of coagulating salts (Cf. Chapter XIII). The present edition has been almost entirely rewritten and the literature has been brought down to the middle of 1917.

In conclusion I wish to express my very great indebtedness to my wife, for her assistance in preparing the manuscript for the press, to Dr. Hardolph Wasteneys for his assistance in proof-reading, and to Dr. C. L. A. Schmidt for his assistance in proof-reading and in the verification of many references and formulæ.

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BERKELEY, CALIFORNIA,
Nov. 1, 1917.

* von Schroeder, P., *Zeit. f. physik. Chem.*, 45 (1903), p. 75. Dietz, W., *Zeit. f. physiol. Chem.*, 52 (1907), p. 279. Cf., however, Chapter XVII.

† Cf. for example, W. Sutherland, *Phil. Mag. Series 6*, 14 (1907), p. 1.

‡ "Die physikalische Chemie der Proteine," Dresden, 1912. Theodor Steinkopff.

THE PHYSICAL CHEMISTRY
OF
THE PROTEINS

"From the point of view of the physicist, a theory of matter is a policy rather than a creed; its object is to connect or co-ordinate apparently diverse phenomena, and above all to suggest, stimulate and direct experiment. It ought to furnish a compass which, if followed, will lead the observer further and further into previously unexplored regions. Whether these regions will be barren or fertile experience alone will decide; but, at any rate, one who is guided in this way will travel onward in a definite direction, and will not wander aimlessly to and fro." J. J. Thomson, "The Corpuscular Theory of Matter."

THE PHYSICAL CHEMISTRY OF THE PROTEINS

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FOURTH AVENUE & 30TH STREET, NEW YORK

39 PATERNOSTER ROW, LONDON

BOMBAY, CALCUTTA, AND MADRAS

1920

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First Edition, January, 1918
Reprinted, January, 1920

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DEDICATED TO MY MOTHER
IN AFFECTIONATE ACKNOWLEDGMENT
OF ENCOURAGEMENT AND
INSPIRATION

PREFACE

THE Proteins, with which, as its title indicates, this work has most particularly to deal, have, ever since the publication of the classic researches of Graham, been generally recognized as typical examples of that class of substances which Graham designated "Colloids." This work, therefore, although primarily concerned with the physical chemistry of a limited section of the class, may also, in some measure, be regarded as contributing to an analysis of the properties and behavior of colloids in general, in so far as these permit of illustration by the properties and behavior of the various members of the protein group.

The leading problems in every field of chemical investigation are, to a large extent, determined by the salient properties of the substances which form the subject of inquiry, and for this reason a thorough acquaintance with what may be termed the "descriptive chemistry" of any group of substances is prerequisite to a successful attempt to interpret their behavior. If we were to endeavor to interpret the behavior of the proteins solely in the light of preconceptions derived from the study of the chemistry of the metals, for example, or the simpler organic compounds, we would find that the behavior of the proteins displays merely a bewildering variety of inconsistencies. Their "amphoteric" character, their multiple basicity and acidity, their instability in aqueous solution and, above all, the enormous mass and catenary configuration of their molecules, confer upon them properties which are comparatively unfamiliar in other fields of chemistry or else exaggerate properties which are normally displayed by the simpler chemical bodies only to a comparatively negligible degree.

The proteins in this respect are not exceptional. Thus the mode of investigation and the interpretation of the behavior of the various lipoids must primarily be conditioned by their very general insolubility in water and instability in the presence of oxygen. The behavior of the complex polysaccharides is conditioned by their relative stability and by the extraordinary tendency to op-

tical isomerism which is displayed by the simpler carbohydrate radicals out of which they are built up, while, on the other hand, the behavior of rubber and its congeners is primarily conditioned by the enormous internal molecular friction which leads them to display, to an exaggerated extent, phenomena analogous to hysteresis which, although not wholly negligible in other colloids, for example in the protein group, nevertheless seldom present themselves as salient characteristics of their behavior.

The colloids are therefore an exceedingly heterogeneous group, the only common distinguishing characteristic being the relatively enormous mass and volume of the molecules of the most "typical" representatives of the class, and of course as many gradations of behavior exist as there are gradations in the mass and volume of molecules. Nothing is to be gained, therefore, by endeavoring to force the various members of the colloid group into artificial conformity with definitions which are designed to separate them, as if they were a homogeneous group, from other classes of chemical substances. To describe a particular property or mode of behavior as a "colloidal phenomenon" neither defines nor interprets it and furthermore fails even to describe it, since there are no phenomena which are distinctively "colloidal" and displayed by every member of the colloid group, saving only those phenomena which depend primarily upon the simple factor of the mass or volume of the molecules, and which are therefore predictable from and implied in the properties or behavior of the smaller molecules of the non-colloidal substances.

Similarly, the use of the term "adsorption" to describe the union between colloids and other substances implies a uniformity where no uniformity exists and is, moreover, devoid of utility or meaning unless we attach to the definition some distinct idea of the nature of the underlying forces which condition the union, whether these forces be regarded as consisting of chemical (*i.e.*, atomic) attractions or of capillary (*i.e.*, molecular) attractions. But in forming such concrete ideas we are simply returning to conceptions which are already familiar to us in the "crystalloid" field of chemistry and which call for no definitions which we do not already possess as the result of our general acquaintance with the physical and chemical phenomena which are displayed by simpler and hitherto more familiar substances.

The investigations of recent years, not only upon the behavior

of the proteins, but upon that of the colloids in general, have resulted in the development of two rather sharply differentiated schools of opinion. The one school endeavors, so far as technical difficulties permit, to directly apply, with modifications suggested by the properties and structure of the particular colloid under investigation, the known laws of what may be termed "molecular" physical chemistry to protein and other colloidal systems, while the other school hesitates to do so. The essential question at issue between these two schools, in so far as the proteins are concerned, is, I think, simply this: Are we justified in assuming that the rule of Avogadro is applicable to protein solutions or are we not? In other words, are protein solutions molecularly dispersed systems or are they, rather, suspensions or emulsions? The latter of the two schools to which I have referred avers from *à priori* considerations, implicitly or explicitly, that Avogadro's rule may not be applied to protein solutions, or, at least, that its validity for these solutions should be established before we venture to apply it. The former school prefers to assume that Avogadro's rule does apply to these systems until actual inapplicability demonstrates that it does not. Now the "proof" of the applicability of Avogadro's rule to systems which are admittedly molecularly dispersed has never consisted in anything but the applicability, to these systems, of laws and deductions founded upon Avogadro's rule. The procedure of the former school would appear, therefore, to be sound and well justified by scientific precedent. Following this procedure we will be enabled to correlate and interpret the phenomena which are exhibited by such protein systems as may chance to be molecularly dispersed, while, on the other hand, we shall be enabled to accurately delimit the conditions under which molecularly dispersed protein systems exist and those under which they do not.

In this work I have endeavored to interpret the physico-chemical behavior of the proteins in the light of the laws of Boyle and of Gay-Lussac, as they have been applied to solutions by van't Hoff, and of the Guldberg and Waage mass-law which, as Larmor has shown, is a direct consequence of Avogadro's rule and Boyle's law.* I have also assumed the validity, in protein systems, of the first and second laws of heat, albeit the applicability of the

* Larmor, J., Phil. Trans. Roy. Soc. London, 190 A (1887), p. 276. T. Brailsford Robertson, Journ. Physical Chem., 10 (1906), p. 521.